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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/847,232	05/02/2001	Ning Huang	0665-0018.30	5945

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EXAMINER

BAUM, STUART F

ART UNIT	PAPER NUMBER
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1638

DATE MAILED: 01/09/2003

9

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/847,232

Applicant(s)

HUANG ET AL.

Examiner

Stuart F. Baum

Art Unit

1638

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 15 October 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☐ Claim(s) 18-22 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) 18-22 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on with application is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____. 6) ☐ Other: _____

DETAILED ACTION

1. Claims 18-22 are pending.

Applicant's election without traverse of Group III, claims 18-22 in Paper No. 8 is acknowledged.

Claims 1-17 have been canceled.

Claims 18-22 are examined on the merits.

Information Disclosure Statement

2. A signed copy of PTO-1449 is included with the present office action.

Specification

3. Objection is made to the specification for not incorporating SEQ ID NO's when referring to nucleic acid or amino acid sequences. 37 CFR 1.821(d) requires the use of the assigned sequence identifier (e.g. SEQ I.D. NO: X) in all instances where the description or claims of a patent application discuss sequences (see page 31, line 33 for example).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Art Unit: 1638

4. Claims 18-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 18, 2nd line, it is not clear what object is being referred to with the recitation “it”.

Is Applicant referring to the seed-specific promoter or the transcription factor?

In claim 18, the metes and bounds of “native state” have not been defined.

In claim 18, the recitation of “increase” lacks a comparative basis.

In claim 18, the recitation “an increase in the activity of said seed specific promoter” is unclear and confusing. The word “activity” is used in conjunction with proteins and is not used in conjunction with promoters.

In claim 19, the term “modified” is unclear. Applicant needs to explicitly state how the seed-specific promoter has been changed. All subsequent recitations of “modified” are also rejected.

In claim 20, the recitation “an increase in the activity of said promoter” is unclear and confusing. The word “activity” is used in conjunction with proteins and is not used in conjunction with promoters.

Scope of Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Art Unit: 1638

5. Claims 18-22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a rice glutelin 1 (Gt1) promoter operably linked to a reporter gene coding sequence in which a 98 bp *Oryza sativa* bZIP (Reb) upstream activation sequence (UAS) fragment containing three copies of GCCACGT(C/A)AG was inserted at position -630 bp distal to the TATA box of the Gt1 promoter co-transformed into rice endosperm with a Reb coding sequence and promoter to increase expression of the GUS gene when compared to GUS expression in endosperm cells only transformed with the UAS-Gt1::GUS construct, does not reasonably provide enablement for claims broadly drawn to any modified seed-specific promoter or a method of making a seed-specific promoter responsive to any transcription factor both of which comprise any seed specific promoter which is responsive in any manner to any transcription factor and inserting any sequence which elicits any response into any position of the seed-specific promoter, to produce a promoter with activity . The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claimed invention is not supported by an enabling disclosure taking into account the *In re Wands* factors (858F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988)). *In re Wands* lists a number of factors for determining whether or not undue experimentation would be required by one skilled in the art to make and/or use the invention. These factors are: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples of the invention, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claim.

Given the indefinite claim language as stated in the previous 112 2nd rejections, the Office interprets the claims to be broadly drawn to a method of making a seed-specific promoter that responds in any way to a transcription factor to which the seed-specific promoter does not respond in an undisclosed state, and determining the native response sequence for the transcription factor and operably linking said responsive sequence to the seed-specific promoter thereby producing a seed-specific promoter that responds in any way to the transcription factor and a plant comprising the seed-specific promoter. Applicants also claim a seed-specific promoter prepared by the above method and a seed-specific promoter wherein the seed-specific promoter is the Gt1 promoter and said transcription factor is Reb.

Applicants have isolated a sequence from the rice globulin (Glb) promoter to which binds the Reb protein. Applicants have disclosed this sequence which contains the motifs GCCACGTCAG and GCCACGTAAG(GCCACGT(A/C)AG) (page 31, lines 26-36) and have inserted this sequence into a particular position of the seed-specific Gt1 promoter (page 31, lines 13-19). Applicants have not taught or disclosed any seed-specific promoter, or any transcription factor whose binding to any seed-specific promoter will increase any response of the promoter compared to the same promoter sequence in which the transcription factor is not bound. In addition, Applicants have not taught any UAS inserted anywhere in any seed-specific promoter that binds any transcription factor to increase any response.

What Applicants have described is a transactivation-like system which utilizes a transcription factor that acts in trans to bind to a cis-acting element that has been incorporated into a promoter. In the present application, the promoter is any seed-specific promoter. Schwechheimer et al (2000, *Funct Intergr Genomics* 1:35-43) teach transactivation systems have

Art Unit: 1638

inherent problems which leads to unpredictability within the system. They report “Many genes encoding transcriptional activators are differentially expressed or activated in different tissues at different stages of organismal development or in response to environmental stimuli” (page 35, right column, 1st paragraph). In addition, “numerous transcriptional activators vary in their strength and possibly in some cases also in their tissue-specific activity” (page 41, left column, 2nd paragraph). They also report that target gene silencing is a problem that can occur if there is a high concentration of transcription factors within the nucleus (page 41, right column, 1st paragraph) or that the upstream activation sequences become methylated. Schwechheimer et al state “It has been postulated that the GAL4-promoter binding sites may be methylated and that methylation interferes with promoter activity” (page 41, right column, 1st paragraph). Schwechheimer et al also teach that not all promoters confer the same level of expression in all plant system (page 36, left column, 2nd paragraph).

Applicants have claimed a method of making a seed-specific promoter, a modified seed-specific promoter and a seed-specific promoter produced by the method comprising inserting a response sequence anywhere within the seed-specific promoter. But, inserting it anywhere will lead to deletions, substitutions or rearrangements within the original seed-specific promoter which cannot be expected to maintain the original promoter or enhancer activity, or to have any activity. Izawa et al (1993, J. Mol. Biol. 230 :1131-1144) teach the nucleotides flanking the G-box (CACGTC) and C-box (GACGTC) hexameric cores were shown to affect protein binding activity and specificity of bZIP transcription factors (of which Reb is a member) (page 1132, bottom of right column; page 1134, bottom of left column). Hao, et al (1998, The J. of Biological Chemistry 273 (41): 26857-26861) investigated the binding activities of ethylene-

Art Unit: 1638

responsive element-binding proteins (EREBP) to their cis-element GCC box (AGCCGCC).

Creating base-pair substitutions within the GCC box modulates binding specificity, implying that different positions within the GCC box are important for differential binding by different EREBP's, in particular, substituting T's for the two G's eliminates binding completely (*supra*, pages 26857, abstract and 26860, left column, 2nd paragraph). Given the rationale set forth above, Applicant is not enabled for a seed-specific promoter, a modified seed-specific promoter and a seed-specific promoter produced by the method comprising inserting a response sequence anywhere within the seed-specific promoter.

Not only are DNA sequences located 5' to the translation start site (ATG) sensitive to base changes, but in some instances, intronic regions have been shown to be necessary for proper gene expression. Even though the present application does not claim intronic regions, this evidence is presented to demonstrate how a two base pair deletion or alteration of a cis-acting region can affect the binding of trans-acting factors that are important for proper spatial and temporal expression of a respective gene. Busch et al (1999, Science 285:585-587) and Lohmann et al (2001, Cell 105 :793-803) teach *LEAFY* (*LFY*) and *WUSCHEL* (*WUS*), which have been shown to be transcription factors that together activate proper *AGAMOUS* (*AG*) expression, do so by binding to the second intron of the *AG* gene. A two base-pair mutation within the binding site of either *LFY* or *WUS* eliminates binding of either *LFY* or *WUS*, respectively (Busch et al (*supra*) page 587 left column, 2nd paragraph; Lohmann et al (*supra*) page 799, bottom and top of left and right columns) and changes the temporal and spatial *AG* expression pattern.

Art Unit: 1638

Applicants are not enabled for any seed-specific promoter or any transcription factor given the disclosed Gt1 promoter and Reb transcription factor are not representative of all seed specific promoters and all transcription factors, respectively. One would not know how to identify all response elements or seed-specific promoters, or where response segments should be inserted in another seed-specific promoter based upon the insertion position and segment of a single promoter in Applicant's disclosure.

Given the unpredictability of creating a seed-specific promoter comprising any response sequence that binds any transcription factor and still retains the correct spatial and temporal expression pattern as was observed before the random introduction of the response sequence into the promoter for the reasons stated above; given the unpredictability of creating such a seed-specific promoter and having it respond in a desired way; given the lack of guidance and examples of selecting a seed-specific promoter, a transcription factor with associated response sequence and inserting the response sequence in any location within said seed-specific promoter sequence so that the selected transcription factor will bind to the promoter sequence to cause any response of the seed-specific promoter; given the state of the art that teaches transactivation UAS's are unpredictable for continued expression because of nucleic acid methylation as discussed above; and given the broad recitation of the claims which encompasses more than what Applicants have taught, it would require undue experimentation by one skilled in the art to make and/or use the claimed invention.

Written Description

6. Claims 18-20, and 22 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to a method of making a seed-specific promoter that responds in any way to a transcription factor to which the seed-specific promoter does not respond in an undisclosed state, and determining the native response sequence for the transcription factor and operably linking said responsive sequence to the seed-specific promoter thereby producing a seed-specific promoter that responds in any way to the transcription factor and a plant comprising the seed-specific promoter. Applicants also claim a seed-specific promoter prepared by the above method and a seed-specific promoter wherein the seed-specific promoter is the Gt1 promoter and said transcription factor is Reb.

The Federal Circuit has recently clarified the application of the written description requirement. The court stated that a written description of an invention “requires a precise definition, such as by structure, formula, [or] chemical name, of the claimed subject matter sufficient to distinguish it from other materials.” *University of California v. Eli Lilly and Co.*, 119 F.3d 1559, 1568; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). The court also concluded that “naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material.” *Id.* Further, the court held that to adequately describe a claimed genus, Patent Owner must describe a representative number of the

Art Unit: 1638

species of the claimed genus, and that one of skill in the art should be able to “visualize or recognize the identity of the members of the genus.” *Id.*

In the instant application, Applicant is claiming any seed-specific promoter, any transcription factor and any responsive sequence to which the transcription factor binds. Given the claim breadth and lack of guidance as discussed above, the specification fails to provide an adequate written description of the genus as broadly claimed. Given the lack of written description of the seed-specific promoter, transcription factor and responsive sequence, and any method to combine all of the before mentioned parts would also be inadequately described. Accordingly, one skilled in the art would not have recognized Applicants to have been in possession of the claimed invention at the time of filing. See Written Description Requirement guidelines published in Federal Register/ Vol. 66, No. 4/ Friday January 5, 2001/Notices: pp. 1099-1111).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 19 and 20 are rejected under 35 U.S.C. 102(b) as being anticipated by Nakase et al (1997, Plant Molecular Biology 33:513-522, list in IDS).

The claims are drawn to a seed-specific promoter comprising a promoter sequence that expresses in seeds and further comprising a responsive sequence for a transcription factor that

Art Unit: 1638

when bound causes the promoter to respond in any way to the transcription factor as compared to a response by the promoter when the transcription factor is not bound. In product claims, the method of making holds little patentable weight if the claimed product is indistinguishable from that of the prior art.

Nakase et al teach a rice globulin promoter, which is seed specific, that binds the transcription factor Reb, thereby producing a response in a gel shift assay which is different compared to the response of the promoter without the transcription factor bound, and as such, Nakase et al anticipate the claimed invention (page 518, "Super-shift assay" section).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. Claims 19-20, and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nakase et al (1997, Plant Molecular Biology 33:513-522, list in IDS) as applied to claims 19-20 above, and further in view of Jung et al (December, 1998, U.S. Patent Number 5,850,016).

The teachings of Nakase et al have been discussed above.

Nakase et al do not teach a plant transformed with a seed-specific promoter.

Jung et al teach a plant transformed with a seed-specific promoter (columns 19-22, Examples IV) for expressing a gene of interest in seeds (column 4, lines 15-24).

Art Unit: 1638

Given the recognition of those of ordinary skill in the art of the value of seed-specific promoters for expressing a protein of interest in seeds, one skilled in the art would have been motivated to transform a plant with a seed specific promoter, such as the promoter of Nakase et al., to target protein expression to seeds, using the transformation method of Jung to generate the claimed invention with a reasonable expectation of success.

9. No claims are allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stuart Baum whose telephone number is (703) 305-6997. The examiner can normally be reached on Monday-Friday 8:30AM – 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (703) 306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 or (703) 305-3014 for regular communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the legal analyst, Gwendolyn Payne, whose telephone number is (703) 305-2475.

Stuart F. Baum Ph.D.

December 27, 2002


ELIZABETH F. McELWAIN
PRIMARY EXAMINER
GROUP 1800

for
Phuong Bui